14

p94. - 1886

ANTI-CHOLERA INOCULATION.

c

The English scientific world is dimly aware that a certain Dr. Jaime Ferran, of Tortosa, in Spain, claims to have discovered a method of protective inoculation against cholera, from which—according to his own statements—the most wonderful results have accrued. But Britain is proud to remember that even the renowned Koch's discovery of the so-called cholera bacillus received its ignominious deathblow from Dr. Klein, a naturalised Englishman, the commissioner of our Government, who swallowed the organism by the tumblerful with absolute impunity. We know further, in a vague and misty way, that Ferran's whole superstructure professes to be based on Koch's discredited discovery. We know that good things don't come out of Nazareth, and that Spain is the last country in Europe to which we can look for scientific light. When, therefore, medical journals tell us that serious consequences and even deaths have resulted from these inoculations—when the *Times* informs us that there can be little doubt but that Ferran's credulous patients

> are subjected to some form of septic poisoning, the effects of which would be likely to vary with the state of health of the recipient, but that there is not a tittle of evidence to show that the fluid used for the inoculation is capable either of producing cholera or of conferring immunity from it;

that at best, in fact, the whole thing is

> but the outcome of an hypothesis founded upon another hypothesis, to which scientific opinion in this country is now altogether opposed;[1]

—when we are gravely informed of all this, most of us are quite ready to put the whole thing aside as unworthy of attention, and to admit with the writer in our great national foolometer that

> Ferran's experiments and the talk about them are alike to be deprecated, inasmuch as they serve to excite expectations not likely to be realised, and in this way to divert attention from means which experience has proved to be absolutely necessary

for the protection of our country against cholera.

But the world moves, even though we may shut our eyes to the fact and pooh-pooh it as a mere hypothesis. For my part I prefer to examine evidence instead of ignoring it, and looking at the evidence regarding Ferran's discovery, and comparing it with what can be adduced in support of the discovery of Jenner, I have not the slightest hesitation in saying that that evidence is as ample as it could well be made during the six months which have elapsed since Ferran inaugurated his system on himself, and that it is infinitely more crucial and convincing than anything which Jenner could bring forward ten years after his first experiment on his son.[2] Close on a century has elapsed since then, and with all our accumulated experience what are the facts on which we now found our belief in the efficacy of Jennerian vaccination? According to Dr. Buchanan, Chief Medical Officer to the Local Government Board, the population of the metropolis in 1881 consisted of 3,620,000 persons who had been vaccinated, and 19,000 who were unvaccinated. A great epidemic of small-pox had just closed, and during that epidemic 15,171 persons—11,412 vaccinated and 3,759 unvaccinated—had been treated in the hospitals of the Metropolitan Asylums Board. Had small-pox dealt with the unvaccinated section of the population as lightly as it dealt with the vaccinated, instead of furnishing 3,759 cases it should have yielded but 599, or 6⅓ times less. Therefore the vaccinated population exhibited an immunity from attacks of small-pox six and a third times greater than that enjoyed by the unvaccinated. Again, among the 11,412 cases of small-pox in vaccinated persons recorded, there were but 1,008 deaths, while among the 3,759 unvaccinated there were 1,669. If the death-rate among the unvaccinated cases had been as low as it was among the vaccinated there would have been but 332 deaths instead of 1,669, or 5 times less. From this it follows that when small-pox does occur among vaccinated persons the probability of recovery is five times greater than in unvaccinated persons; and multiplying the two protections together, the chance of not dying from small-pox is about 31½ times greater among the vaccinated population than it is among the unvaccinated. Well, how does the protection conferred by Ferran's procedure contrast with this? Before answering that question let me first explain the nature of his great test experiment.

---

[1] The *Times*, July 2, 1885.

Dr. Ferran had proved the theoretical portion of his case by demonstrations, which I shall afterwards describe, when the outbreak of cholera at Alcira afforded him the opportunity of putting his theories practically to the proof. Alcira is built upon a small island in the river Jucar, and according to the official census contains 16,000 inhabitants. On the 27th of April cholera appeared in the town, and on the 1st of May Dr. Ferran had established himself there and set to work. He had no compulsory law to assist him, and was frowned on by the Government, whose measures of quarantine he had scoffed at. But though a comparatively young man, his reputation for learning had spread through Catalonia and Valencia. The municipality of Barcelona had last year sent him as their representative to Marseilles to study the cholera epidemic which ravaged the South of France. He had written on cholera, and had propounded a treatment of which he had proved the harmlessness on himself and fifty of his friends, and a commission named by the Barcelona Academy of Medicine had verified his statements and results. The inhabitants of Alcira were panic-stricken and ignorant, and when Dr. Ferran presented himself in their midst, they eagerly flocked to him for aid. He prosecuted his work systematically. Every man, woman, and child inoculated received a certificate filled up with his or her name, and bearing a number corresponding with an entry in a register of cases which he kept. On the back of the certificate were printed half a dozen short paragraphs stating what was actually claimed for the system. It would not, the reader was informed, confer absolute protection against cholera any more than vaccination conferred absolute immunity from small-pox, but it would greatly diminish the chances of attack, and still more so the risk of death. The protection, too, would probably wear out, and inoculation should therefore be repeated from time to time during an epidemic. One paragraph I shall give entire :—

---

[2] In November 1789. See Baron's *Life of Jenner.*

> As the inoculation requires a certain time to ensure the immunity of the person inoculated, it should be noted that every attack of cholera occurring during the first five days after inoculation is outside its influence, which cannot be relied on before the expiration of five days.

This *caveat* against including in the statistics collected deaths occurring within five days after the operation was—it will be seen from the above—clearly put in at the very commencement of the experiment.

On the 18th of May Dr. Ferran telegraphed me that up to that date 5,432 of the inhabitants of Alcira had been inoculated, leaving some 10,500 uninoculated. Among the uninoculated population there had been 64 cases of cholera, or 1 in every 163 persons, and 30 deaths, or 1 in every 352. Among the inoculated there had been but 7 attacks, or 1 in every 776 persons, and no deaths. These are sufficiently brilliant results, but I propose to give Ferran the trial of a pickpocket, and shall not accept a single statement he makes unless supported by independent testimony. I therefore at once turn to the evidence of his professional brethren, and take my stand upon it.

Le Temps of the 27th of June contains a report issued by the Medical Corps of Alcira, and attested by eleven signatures. From this report I extract the following tables :—

Table from May 1 *to May* 31 *inclusive.*

Official census of inhabitants . .	16,000
Inoculated	7,043, or 44·01 per cent.
Re-inoculated	4,117, or 25·73 per cent.

	Uninoculated	Inoculated	Re-inoculated
Attacks	121	14	9
Recoveries	49	10	8
Under treatment	15	1	1
Deaths	57	3	0

Observation.—In no case did a death of an inoculated person occur after the fifth day. One of the fatal cases, when inoculated, had already premonitory diarrhœa.

Table from June 1 *to June* 17 *inclusive.*

Inoculated	8,874, or 55·46 per cent.
Re-inoculated	5,210, or 32·56 per cent.

	Uninoculated	Inoculated	Re-inoculated
Under treatment since May	15	1	1
Attacked during June	71	10	8
Recoveries	26	8	7
Under treatment	15	1	1
Deaths	45	2	1

Observation.—One of the inoculated cases died within five days after inoculation.

Neither these tables nor the report which accompanies them enables one to say whether the Medical Corps includes re-inoculated cases with inoculated. To assume that in these statistics re-inoculations are not included in the inoculations, would be the view of the case enormously the more favourable to Dr. Ferran, and I shall therefore assume the other alternative, namely, that the number of inoculated (including re-inoculated) at the 31st of May was but 7,043, and at the 17th of June 8,874. The mean of these two figures, 7,958, will then be the mean number of inoculated of all classes exposed to the epidemic influences prevalent at Alcira during the eighteen days from the 1st of June to the 17th of June inclusive. Well, here we have the typical conditions of a crucial test experiment, precisely similar to that which Pasteur himself devised to prove the efficacy of his anti-anthrax vaccination—an isolated town of 16,000 inhabitants divided into two equal batches, consorting together for precisely the same time under precisely similar conditions, and exposed to precisely the same exciting causes of disease. And what, on the testimony of the Medical Corps of Alcira, was the result? Tabulated for easy comparison with the foregoing tables it was this :—

Results from June 1 *to June* 17 *inclusive.*

Mean number of inoculated (including re-inoculated) persons	7,958, or 49·74 per cent.
Mean number of non-inoculated persons	8,042, or 50·26 per cent.

	Uninoculated	Inoculated
Attacks	71	18
Deaths (eliminating in inoculated cases deaths during five first days)	45	2

In other words, 1 case of cholera occurred in every 113 persons among the uninoculated population and 1 in every 442 in the inoculated, or four times as few in proportion. Among the uninoculated persons attacked, 2 out of every 3 died, among the inoculated but 2 out of 18, or six times as few. Among the uninoculated population 1 person in every 179 died of cholera, among the inoculated but 1 in 3,979, or a proportion smaller by twenty-two and a quarter times. Here then we are in a position to compare the protective efficacy of vaccination against small-pox, and inoculation against cholera, to a nicety. The immunity exhibited in the two instances I have detailed by populations protected against small-pox and cholera by the methods of Jenner and Ferran respectively was this:—

	Small-pox	Cholera
Security against attack enjoyed, compared with unprotected population	as 6⅓ to 1	as 4 to 1
Security against death if attacked . .	„ 5 „	„ 6 „
Security against a fatal attack . . .	„ 31½ „	„ 22¼ „

These are far from the maximum results attainable under the working of Jenner's vaccination, but they are the results actually attained under State encouragement of the most exceptional kind and three-quarters of a century's experience. In the case of Ferran's inoculations, the results are those obtained without experience, in the midst of extraordinary pressure, by the energy of a single man and in the face of State opposition. It is of course open to assert that the eleven gentlemen who signed the tables I have quoted are active or passive parties to the fraud of palming off cooked statistics on the public. But that involves four further assumptions—(1) that Dr. Pulido, of Madrid, who in the *Siglo Medico* of the 7th of June gives correspondingly significant figures regarding 1,851 cases of inoculation in other towns, is in league with them; (2) that Drs. Galvan, Lierandi, and Hernandez, of Benifayo, and Dr. Segui, of Cheste, who testify to similar figures in the case of their respective towns (not included in Pulido's statistics, are parties to the deception; (3) that the medical commission named by the Provincial Representatives of Albacete, which reported 'that the inoculation has a prophylactic value, demonstrated scientifically by facts,' sails in the same boat with the rest; and (4) that the Commission of the Barcelona Academy of Medicine, which testified to corresponding results in experiments on animals, was probably little better than the others. If we carry our incredulity so far, there is no proof that Ferran's procedure is better than a fraud, but then applying the same test to vaccination against small-pox, we are driven to precisely the same conclusion.

Admitting the same evidence as to results in the two cases, the correctness of the theory of the mode in which those results are obtained is as immaterial in the one case as in the other. The vaccine lymph which we use may be simply small-pox modified by transmission through the cow, as our authorities hold, or it may be some-thing entirely different, as the exhaustive experiments of Chauveau appear to me to prove. In the same way the cholera vaccine manufactured by Dr. Ferran may consist of pure cultures of the cholera-bacillus, as he maintains, and as the Barcelona Commission asserts, or it may simply consist of 'some form of septic poison,' as others suspect. But if 'some form of septic poison' or septic organism was found to have the effect alleged, it would not be one whit more astonishing than the fact that fowls, which Pasteur had artificially infected with cattle-anthrax, afterwards proved refractory to chicken-cholera; or, if Chauveau's demonstration of the absolute non-identity and non-transmutability of cow-pock and small-pox be correct, than that inoculation with cow-pock confers immunity from small-pox. But if the theory on which Ferran's method professes to be based should prove to accord with the generally accepted theory of vaccines—viz., that they are modifications of the virus of the disease against which they protect, and that they confer immunity in proportion to the immunity from second attacks conferred by the disease itself—his case would be simplified and strengthened.

The first theoretical objection to Ferran's procedure from the standpoint of theory is that cholera does not protect against second attacks, and that therefore the pretence of protection arising from a modified type of the disease is absurd. Now, in order to extinguish Ferran by proving that cholera itself does not protect against second attacks, Surgeon-General Murray, M.D., published in the *St. James's Gazette* of the 8th of last June an elaborate table of statistics setting forth the cholera experience of the Central Gaol of Agra from 1860 to 1865, and he will probably be surprised when I appeal to his figures to prove exactly the converse of his proposition. Of course I don't mean to say that cholera confers absolute immunity from second attacks—neither does small-pox, nor scarlatina, nor measles—but what I say is, that for a time cholera, like the other diseases I have named, does confer a comparatively great immunity from attack. Out of an average strength of 2,364 prisoners, in the course of the five epidemic years 1860-5, there were, Dr. Murray tells us, 1,196 admissions of cholera cases and 304 deaths, and of these 63 cases were admitted a second and 5 a third time. Deducting the double and treble admissions, we have 1,128 prisoners attacked, and among these (again deducting the deaths in secondary and tertiary cases) there were 271 deaths. In other words, 1 prisoner out of every 2·09 on the average strength was attacked, and 1 out of every 8·72 on the average strength died. 857 recovered, and of these 63, or 1 in every 13·6, was attacked, and 30, or 1 in every 28·56, died. During a period extending over five years, therefore, the immunity from attack among the cholerised prisoners was four times as great as it was among the uncholerised, and the immunity from fatal attack was 3·05 times greater. But the immunity conferred by inoculation of all kinds—small-pox, anthrax, or anything else—tends to wear out, and Ferran claims nothing more than to confer comparative immunity for a few months. What do Dr. Murray's figures teach us concerning second attacks occurring within a year after the first? Why this, that out of a mean average strength of 875 cholerised prisoners only 35 attacks occurred within twelve months after cholerisation, or 1 in every 25 persons, and 16 deaths, or 1 in every 54·66 persons. The immunity exhibited by the cholerised population from attack within twelve months, therefore, was nearly twelve times as great as that exhibited by the non-cholerised, and the immunity from fatal attack within the same time was 6·19 times as great. These results entirely justify the principle on which Ferran's procedure professes to be based, and the only point on which they appear to disagree with his results is in the high mortality which they exhibit in cases of second attack. But the disagreement is of no import, as it does not follow that the cholera virus falling on organs damaged by a previous natural attack will prove as little dangerous as when the first attack has been artificially contrived to fall on a totally different portion of the system. That we can artificially control and divert the incidence of diseases producible by inoculation we know by ample experience. Small-pox inoculation is a case in point. Small-pox as taken in the ordinary manner by unprotected persons is a horrible, deadly disease. Introduce the virus into the skin, and the manifestations of the disease are so trifling as to be, as Jenner tells us, often undistinguishable from cow-pock. Pasteur can, by different methods of introducing the virus, produce different forms of hydrophobia, with symptoms varying from 'dumb' paralysis to raging delirium. Chauveau, by injecting cow-pock virus into the blood-torrent in arteries, produced not a localised but a general eruption. And similar results can be obtained in chicken cholera, the bovine disease known as the 'maladie de Chabert,' and doubtless in a host of other diseases which have yet to be worked out.

Having disposed of this preliminary objection, then, let us examine the theoretical basis of Ferran's alleged discovery, and see how it accords with the teachings of science in other analogous cases. But this will necessitate a digression and an explanation which I shall endeavour to make intelligible to the most unscientific mind.

The researches of modern scientists, and notably those of Pasteur and Tyndall, have proved that, besides its visible animal and vegetable inhabitants, this world swarms with a population of living entities of extreme minuteness, detectable only under strong powers of the microscope, and requiring special treatment and staining to render them perceptible even then. These entities possess most of the distinctive characteristics of vegetable life, but many of them are full of energy and motion, wriggling and gliding and swimming about in the fluid in which they live, so that for long it was a question among philosophers to which of the great divisions of life they really belonged. To get rid of dispute on this preliminary point, Sedillot devised for these microscopic organisms the non-contentious name of 'microbes,' or minute living beings, and that name, being adopted by Pasteur, has become classic in every tongue. The world of microbes counts as many and as diversified families and races as there are races and families of visible plants and animals. We may be sure of so much, and we have good grounds for the belief that the species of microbes are incomparably more numerous than anything to be found among their grosser fellow dwellers on the globe. Their habits, forms, and functions are infinitely varied. They are to be found everywhere, and performing all kinds of work. Microbes ferment our bread, turn wort into beer, grape-juice into wine, and wine into vinegar. Microbes cause meat to putrefy, milk to become sour, and butter rancid. Exterminate the microbes in our fields, and they would produce no crops, and without the aid of the hosts of microbes who find their habitation within ourselves, it seems highly probable that the digestion even of the ploughman would come to a stop, and that food would be to us as a poison. On the other hand, could certain mischief-working microbes be banished from the world, smut, and rust, and mildew would disappear from our fields, and small-pox, typhoid, consumption, leprosy, yellow-fever, and a host of other scourges would cease to afflict the abodes of men. These microbes propagate themselves by budding or subdivision, and by the production of spores (or rudimentary seeds), and under favourable circumstances they do so with such extraordinary rapidity that a single individual will give rise to myriads in the course of twenty-four hours; and during one revolution of the earth a greater number of generations will have sprung into life than man can boast of since the days of Adam. Can it be wondered therefore that in the microbe world the struggle for existence is at its fiercest, and the capacity for change of character and habits under artificial cultivation is found to exist to an extent undreamt of, in the regions of higher and consequently slower life? For many or most of these microbes are omnivorous feeders, and can be reared not only on animal or vegetable substances, but will at a pinch flourish in solutions of appropriate organic salts, and in different media the same species will rapidly exhibit very different habits of size and growth, and even of propagation, and give rise to very different products. Especially is this the case when cultivation in different temperatures and with differing exposures to light and air are brought into play, but on that point alone a book might be filled with the curious knowledge that has been accumulated concerning them. Reared in animal or vegetable juices or decoctions, the difficulty is to keep a single species pure, and all kinds of devices have to be resorted to to guard the medium in which it lives from the contamination of floating germs from without. But in gelatine they can be easily separated and reared in purity. Dozens of different microbe species and families might last year be seen side by side, growing under the auspices of Dr. Watson Cheyne, in tubes of gelatine at the Health Exhibition, and those who studied them will easily understand how experts can recognise a particular microbe by its habit of growth when so placed. One flourishes most vigorously towards the air, another in the jelly's depths ; one liquefies the medium on which it feeds, another leaves it solid ; some reduce the jelly to a coloured and others to an opalescent fluid, while yet others remain visible simply in the form of fleecy clouds. Well, long ere Pasteur had demonstrated the identic processes of fermentations and diseases, their analogy had been more than suspected, and cholera was among the diseases most evidently dependent on a process analogous to that of fermentations. When the dependence of diseases upon different specific microbes had been demonstrated in one or two cases, it was evident that there must be a microbe which, invading the system, was the cause of cholera ; and Koch, who had first succeeded in cultivating and studying outside the body the microbe-factor of anthrax, the deadly bovine disease to which I have already referred ; Koch, who had afterwards unmasked and isolated the microbe-cause of consumption in man, set himself to work to discover the microbe-cause of cholera. And he discovered it in an infinitely minute organism with whose renown the world has since rung, the famous comma-bacillus. A bacillus is simply a form of microbe so called from its resemblance to a little rod, and Koch called this particular bacillus the comma-bacillus, because it was curved like a comma (,). He invariably found it—though other investigators were not so successful—in cholera cases, and he never found it—though other investigators said they did—in any other disease. Other men produced other comma-shaped microbes, which they found in all sorts of places—in marshy water, in decaying cheese, in healthy human saliva, in morbid secretions and tissues of various kinds—but Koch stuck to his point, and maintained that these were not his comma-bacillus, and that their behaviour under cultivation proved that they were entirely different. But he failed to establish his case by the rigorous proof required to establish as a scientific fact the connection of cause and effect between his comma-bacillus and cholera. He isolated and cultivated his organism—a lively, delicate, and interesting microbe, by the way—and he even discovered it in the water used in a cholera-stricken district, but he utterly failed to reproduce the disease in animals, introduce the bacillus into their systems how he might, and the world considered that his views and his microbe had alike received their *coup de grâce* when Dr. Klein, sent by the British Government to India to investigate the discovery, swallowed full doses of the comma-bacillus and found himself none the worse. Koch's renown as an experimenter was such, that when he declared that his innumerable attempts to communicate cholera to the lower animals, conducted in Egypt and India, had produced only negative results, and that he believed the brute creation to be insusceptible of it, the scientific world considered the matter settled. Former experimenters of repute in Europe had alleged that they had imparted cholera to various lower animals, but they must have been mistaken. And when again, after the publication of Koch's reports, cholera having once more established itself in Europe, MM. Nicati and Reitsch, of Marseilles, announced that they had succeeded in producing cholera by the injection into guinea-pigs of pure cultivations of Koch's comma-bacillus, their report was received with incredulity. But when the same result was achieved by Dr. Van Ermengem, of Brussels, by Drs. Doyen and Babes, of Paris, and by a dozen other investigators in Italy and elsewhere, and finally, when Koch himself, returned to Berlin, produced fatal cholera in guinea-pigs by the injection of one-hundredth part of a drop of fluid impregnated with his microbe, the demonstration would have seemed complete had it not been for the harmlessness of Klein's 'microbe dinner,' and of similar performances on the part of other disbelievers in India.

And yet these microbe dinners proved absolutely nothing more than would be proved if a philosophic horse should set himself to show that the parasitic bot-worm had nothing to do with the gadfly, by swallowing a mouthful of the full-grown insect. He would find himself none the worse; but he would have proved nothing, for he had simply swallowed the fly instead of the egg. Recently M. Bochfontaine repeated Klein's experiment in a rougher form in Paris, and swallowed five cubic centimetres of choleraic matter made up into pills. In a few hours his pulse rose from 70 to between 100 and 120. He experienced sleeplessness, nausea, and slight convulsions, and these symptoms lasted for four-and-twenty hours. Probably were Dr. Klein to repeat the experiment—which in India proved so harmless—in the colder latitude of London he might obtain very different results.

On what grounds do I venture on this conjecture? Because of the very different results which in this case the same experiments on the same classes of animals have given when conducted in different climates, and because the discoveries made by Dr. Ferran, and corroborated by the Barcelona Commission, if we provisionally accept them, explain that, as in the case of other microbes, different results may be ensured by the cultivation of the cholera microbe at different temperatures. The puzzling thing about Koch's comma-bacillus, as he described it in India, was how it could possibly do the mischief which he attributed to it. The smallest trace of acid killed it, and the gastric juice of every animal, including Dr. Klein, into whose stomach it was introduced, digested it with perfect ease. The robuster ferments which flourish in sewage speedily choked it out of existence if it tried to establish itself in that unsavoury medium.

Other microbes, or at least their seed or spores, can stand any amount of rough treatment—drying, boiling, freezing—everything, in fact, short of burning. But this wretched comma-bacillus, if only dried for three hours, was rendered as dead as a door-nail. Assuming that under certain circumstances, in which so far it had not been artificially placed, it produced spores, the spores would naturally be expected to survive the perils which the bacillus could not face; but the most assiduous care on the part of Koch and his disciples having failed to induce it to produce spores, they asserted—in defiance, I have always thought, of an overwhelming mass of evidence—that the cholera microbe does not propagate itself by spores, and they supported their position by the statement that certain classes of microbes have never been shown to produce spores. But the more closely the genesis of every living thing has been traced, the more literally has the truth of Harvey's aphorism been proved—*omne vivum ab ovo.* It is not easy to trace the process of spore-production in ferns and mosses. The infantile history of the kangaroo and platypus for long remained a mystery to zoologists, and when it comes to investigating the life-phases of organisms whose adult forms are measured by 10,000ths of an inch, the minuter phases may easily escape the detective eye even of the most powerful microscope.

It has always seemed to me that if the comma-bacillus was really the microbe of cholera it must produce spores, and that sooner or later some form of it analogous to seed would be discovered. On such an assumption only, so far as I can see, can the phenomena of cholera propagation be reconciled with Koch's contention that his bacillus is really the cause of the disease. Well, what Dr. Ferran alleges briefly is, that he has discovered a method of inducing Koch's comma-bacillus to produce spores, and that those spores, like the spores of other microbes, manifest a vitality incomparably greater than the adult form of the organism. Introduced into the stomach they defy the acids of the earlier processes of digestion, and safely reach those portions of the intestine in which their happy hunting ground is placed. Introduced into sewage, they hold their own against those grosser microbes which choke off the comma-bacillus of Koch. As in the case of the frog's egg or the insect's, there issues forth not the frog or the fly, but the tadpole and the caterpillar, beings that flourish where their ultimate forms would die; so from the spore of the cholera microbe, according to Ferran, there issues forth, not Koch's bacillus, but an intermediate form, differing in shape and endowed with a different vitality, which lives and flourishes in circumstances where its bacillar form would perish.

But why, if the existence of these hitherto unknown phases in the life of the cholera bacillus be real, and if during these phases the organism can be introduced into man and animals through the stomach and through the tissues—why did all the elaborate efforts of

Koch in India and of Pasteur's commission in Egypt fail to produce the disease artificially? How came it that Klein survived his microbe dinner? India and Egypt are tropical climates, and we have seen that when repeated in temperate Europe the same experiments have produced diametrically opposite results. The difference is exactly what one would expect if Ferran's discovery be true. For a detailed description of the *technique* which he employs, I refer those who are interested in the matter to Dr. Van Ermengem's newly published work, *Le Microbe du Choléra*, where in one of the appendices they will find a full description of the process (*op. cit.* pp. 334–47). For the general reader it will suffice to say that Ferran takes a particle of a pure cultivation of Koch's comma-bacillus from a colony growing in gelatine, and placing it in a sterilised and watery meat soup leaves it to multiply for from four to six hours in a temperature of 37° C. (about 101° Fahr.) At the end of that time the soup becomes turbid, and two hours after this change it is taken out, an equal portion of similar soup flavoured with bile is added, and the whole is then placed in a temperature of 15° C. (58° Fahr.) At this temperature the new forms appear, which, according to Ferran, are the forms in which the microbe is transmissible to man, and a pure liquid cultivation of these exposed to the influence of oxygen it is which forms his anti-cholera vaccine. Is the microbe in this vaccine attenuated? Ferran says that his microbe can, like that of cattle-anthrax, be attenuated in various degrees, but for purposes of inoculation attenuation is not essential. This is quite consistent with what we know as to inoculation against pleuro-pneumonia in cattle, where the unattenuated microbe, being introduced into the cool tail of the ox, multiplies so slowly as to give rise to a harmless but protective type of the disease. Raise the temperature of the tail by wrapping it in cotton wool, and the microbe developes so vigorously that the attack is of full severity. The cholera microbe is capable of but a languid existence in cellular tissue, and apparently the law of vaccines has been correctly formulated in the phrase, 'Whenever a virus is placed in conditions unfavourable to its development, it constitutes its own proper vaccine.'

Is there anything incredible in the foregoing account of Dr. Ferran's theory and procedure? To a certain extent the independent observations of Dr. Van Ermengem have verified his observations, and the Barcelona Commission has controlled and verified his procedure. Under the eyes of its members the comma-bacillus has been developed into spores and spirillæ, and these again into comma-bacilli. Before their eyes a quantity of the culture of the infective form has been taken and divided into two parts. One, strained through a Chamberland filter, so as to free it from organisms, has been injected into one series of guinea-pigs, and the result has been *nil*. The second, unfiltered, in half the previous doses has been similarly injected into another series of guinea-pigs, and all have died, and from the blood of the infected animals the comma-baccillus has been recovered. But there remained the proof of the prophylactic power claimed by Ferran for his vaccine. Again, before the eyes of the Commission twenty guinea-pigs were taken, ten inoculated and ten not. A week later they were subjected to injections of the same infective cultivation, the inoculated animals receiving it in larger doses. Again the result accorded with the prediction. The whole ten inoculated guinea-pigs lived, the ten not inoculated died. The demonstrations of other experimenters in the field of the causation of disease have stopped short at man. Ferran's did not. In the beginning of December himself and his friend Señor Pauli, the enthusiastic sharer of his researches, had inoculated themselves. By the end of March, others had been added to the list of his inoculated, and the names of thirty-eight—more than half being medical men—may be seen in the *Comptes Rendus* of the French Academy of Sciences for the 13th of April last.

The Commission of the Barcelona Academy of Medicine examined into twenty cases of inoculation, including half a dozen of those just referred to. A number of these experiments were conducted on the persons of medical men, and their effects, described in detail by the victims themselves, are appended to the report. At first and in the majority of cases thus described, the method of protective inoculation practised by Dr. Ferran seems to have been sufficiently heroic. A cubic centimetre (rather less than the cube of half an inch), in two equal portions, was injected into the cellular tissues of the arms. At the seats of inoculation severe pain was experienced, with heat and swelling, lasting from two to eight days before all uneasiness disappeared, but uniformly subsiding without suppuration. The constitutional symptoms varied, but were sometimes alarming, comprising marked depression of temperature, lividity, cramps, and other symptoms of choleraic collapse, and followed by reaction, from which in the course of a day or two, and without any treatment, the patient recovered.

Subsequently Dr. Ferran had recourse to what the Commissioners call the 'gradual method' of inoculation. This consists of the injection of two drops of the vaccine into each arm, followed in eight days by the injection of twice that amount. With this procedure the general symptoms are insignificant or *nil*, and the local pain, though severe for a short time, rapidly disappears, and on the occasion of the second inoculation there are no general symptoms and little local inconvenience. Remarking on what they had witnessed, the Barcelona Commission with much caution stated—

That as to prophylaxis our deductions encourage the hope that a means of averting cholera has been discovered, but that this could not be affirmed except under test of an epidemic.

The required test, as we have seen, was not long wanting, for on the 1st of May the Alcira experiment was instituted, with the results I have already described—the apparent saving of fifty-three cases of cholera and forty-two lives in a population of 8,000 in eighteen days.

Does not this result fit in wonderfully well with the theory and preliminary experiments? But what of the Royal Commission appointed by King Alphonso? Well, it owed its appointment to a decree issued by the Spanish Minister for the Home Department in the end of May, prohibiting inoculation on the ground that it had in several cases resulted in death. The decree excited so much public indignation that the King ordered a commission. Its nomination naturally devolved on the Minister between whom and Ferran it professed to judge, and its composition was such as to lead to the foregone conclusion of a report hostile to the latter. Great was the public astonishment, therefore, when, towards the end of June, it transpired that the Commissioners' Report would be favourable to the system. The Report itself has been shelved by a reference to the Supreme Board of Health and the Madrid Academy of Medicine, but its conclusions have been published, and, as telegraphed to the English press, they are as follows:—

First, the epidemic in Valencia is Asiatic cholera. Secondly, that the comma-bacillus, or microbe, does exist in the liquids used by Dr. Ferran for inoculation purposes. Thirdly, that inoculation is absolutely inoffensive, and ought to be tolerated under State supervision, the State collecting statistics until it can be finally decided if this system is really a preventive against cholera. Fourthly, Dr. Ferran is warmly recommended, as worthy of official protection and assistance, to continue his experiments.

The Report is signed by four Commissioners out of five, the fifth remaining hostile to inoculation, and one, though he signs the Report, deprecates the proposed official intervention,

which has already put such difficulties in the way of the labours of the Commission that it has been unable as yet to pronounce on the efficacy of inoculation.

I have stated the authorities on which I have based what I have written concerning Ferran's alleged discovery. The pieces of the evidence all fit with perfect accuracy into each other, and this causes me to believe them to be true rather than simply the fabrications of a common conspiracy to deceive the world. I have not referred to the unargued denunciations of one or two foreign *savants* of high repute, but hopelessly committed to their own theories, because I have learned from experience that *savants* are, a thousand times more than poets, an *irritabile pecus*, and when they have 'made their book' the greatest of them hates to retract. On the evidence I take my stand, and so far that evidence—which, of course, further evidence may explain or refute—seems to me to point to but one conclusion, namely, that Ferran has discovered a hitherto unknown form of the cholera microbe, and that in that form it can be used as a vaccine hardly less potent against cholera than cow-pock is against variola.

CHARLES CAMERON.

NOTE.—I have read Dr. Brouardel's account of his reception by Dr. Ferran, and have in no way modified my conclusions. Assume the population of Alcira to be 23,000, as he arbitrarily asserts, instead of 16,000, and the result is to reduce the comparative immunity conferred by inoculation from 22¼ to 12 times that exhibited by the uninoculated population. I know too of the incident of the 70 'Little Sisters of the Poor' at Valencia, where 30 were attacked and 16 died of cholera after inoculation; but I have also before me a letter of Señor Enrique Lopez, the medical attendant of their establishment, stating that the disease and the deaths occurred within five days of the inoculation in every case save one, and in that case the nun, having been absent on the 1st of July, when the inoculations took place, was uninoculated. As to Dr. Ferran's alleged refusal to communicate the secret of his preparation, that does not accord with the very complimentary statement of Dr. Van Ermengem as to Ferran's exceptional frankness in communicating his mode of procedure.—C. C.

The Editor of THE NINETEENTH CENTURY *cannot undertake to return unaccepted MSS.*